09:27:35 OCA PAD INITIATION - PROJECT HEADER INFORMATION 08/14/89

Active

Project #: E-25-M95 Cost share #: Rev #: 0
Center # : 10/24-6-Q5459-3A0 Center shr #: OCA file #:
Work type : RES
Contract#: 5 R29 HL39437-03 Mod #: Document : GRANT
Prime #: Contract entity: GIT

Subprojects ? : N
Main project #:

Project unit: ME Unit code: 02.010.126
Project director(s):
KU D N ME (404)894-6827

Sponsor/division names: DHHS/PHS/NIH / NATL INSTITUTES OF HEALTH
Sponsor/division codes: 108 / 001

Award period: 890801 to 900731 (performance) 901031 (reports)

Sponsor amount	New this change	Total to date
Contract value	103,344.00	103,344.00
Funded	103,344.00	103,344.00
Cost sharing amount		0.00

Does subcontracting plan apply ?: N

Title: HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW

PROJECT ADMINISTRATION DATA

OCA contact: Kathleen R. Ehlinger 894-4820

Sponsor technical contact

DR. EDWIN C. GANGLOFF
(301)496-1978
DIV OF HEART & VASCULAR DISEASES
NAT HEART,LUNG,& BLOOD INSTITUTE
BETHESDA, MD 20892

Sponsor issuing office

JANE R. DAVIS
(301)496-7255
DIV OF EXTRAMURAL AFFAIRS
NATIONAL HEART, LUNG, & BLOOD INST.
BETHESDA, MD. 20892

Security class (U,C,S,TS) : U
Defense priority rating : N/A
Equipment title vests with: Sponsor GIT
NONE PROPOSED.

ONR resident rep. is ACO (Y/N): N
NIH supplemental sheet

Administrative comments -
INITIATION OF 3RD YEAR OF PROJECT. CONTINUATION OF E-25-M95.

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 06/29/90

Project No. E-25-M95 Center No. 10/24-6-Q5459-3A0

Project Director KU D N School/Lab ME

Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH

Contract/Grant No. 5 R29 HL39437-03 Contract Entity GIT

Prime Contract No.

Title HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW

Effective Completion Date 900731 (Performance) 901031 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	
Final Report of Inventions and/or Subcontracts	N	
Government Property Inventory & Related Certificate	N	
Classified Material Certificate	N	
Release and Assignment	N	
Other	N	

Comments CONTINUED BY E-25-M48.

Subproject Under Main Project No.

Continues Project No.

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	N
Project File	Y
Other	N
	N

E-25-7095

SECTION IV PROGRESS REPORT SUMMARY	GRANT NUMBER R29HL39437	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Ku, David N.	PERIOD COVERED BY THIS REPORT FROM	THROUGH
APPLICANT ORGANIZATION Georgia Institute of Technology, Atlanta, GA	08/01/90	7/31/91

TITLE OF PROJECT *(Repeat title shown in item 1 on first page)*
Human Atherosclerosis: Role of Pulsatile Flow
(SEE INSTRUCTIONS)

1. Summary of plans for next year of support.

Specific Aims.

1. To quantify the pulsatile flow field for simulated rest conditions in an in vitro model of the human abdominal aorta.

2. To quantify the location and extent of early human atheroma in the abdominal aorta.

Methods. In general, the methods for achieving the goals are not changed from the original grant proposal. Several refinements have allowed us to measure the detailed hemodynamics in an expeditious manner. Magnetic resonance velocimetry has been developed in our laboratory as an accurate, reproducible technique for measuring velocity in the in vitro models. Further developments during the coming year should enable us to make in vivo measurements to verify our laboratory models.

Additional computer graphics software has been developed to integrate hemodynamic information with morphologic measurements to create a three-dimensional display. The morphologic measurements should be easier to obtain and display due to these new computerization techniques.

The in vitro modelling has been refined to include pulsatile flows with physiologic waveforms. The model can simulate postprandial and exercise conditions as well. The hemodynamic environment in the abdominal aorta is dominated by geometry and branch flow division for steady flow. A glass blown aorta model has been constructed based on the average measurements of bi-planar angiograms. The flow system is a constantly recirculating type with water as the working fluid. Pulsatile flow is produced using an adaptation of the flapper nozzle valve, the design of which is presently being patented. The

outflows from each vessel are controlled using precision needle valves. A capacitance bottle is inserted in the outflow system of the iliac arteries to simulate the capacitance of the lower limbs. The flow through the iliac arteries is measured using a Transonic Systems 12 mm cannulating flow probe.

The mean and peak flow rates for the model are scaled to insure dynamic similarity to the in-vivo state. For resting conditions, the Reynolds number is 500. In order to simulate the time dependant flow characteristics of the in-vivo hemodynamics, the model heart rate must be scaled according to the non-dimensional Womersley parameter, $\alpha = (d/2)(\omega/\nu)^{1/2}$ which represents the ratio of unsteady to viscous effects, where ω = frequency of pulse in radians/sec. For typical resting and post-prandial conditions, α is 16. Under exercise conditions, α increases to 23. The triphasic waveform in the infrarenal aorta was duplicated for these experiments. The laboratory model permits an accurate simulation of pulsatile aortic hemodynamics which can be reproducibly controlled.

The next set of studies will quantify the three-dimensional flow field in the abdominal aortic segment under different physiologic conditions of the post-prandial and exercise state. The hemodynamic measurements will be based primarily on Magnetic Resonance Velocimetry. The measurements are obtained on a 1.5 Tesla Whole Body Scanner with a head coil using Gradient Echo sequences. Additional verification measurements will be made with the high resolution, 20 MHz multigate pulsed Doppler ultrasound velocimeter.

Morphology studies will be performed in collaboration with Drs. Seymour Glagov and Christopher K. Zarins at the University of Chicago. Over ten aortas have been harvested from cadavers under pressure perfusion fixation. We will section these arteries for histologic evaluation and quantitation as described in the original grant application. We have added the capability to produce three-dimensional reconstructed images of the sections which will aid us in the correlation of plaque location to specific hemodynamic variables on a point-by-point basis.

2. Results.

The objective of this year's studies was to make quantitative velocity measurements of pulsatile flow in the abdominal aorta under rest conditions. The combination of distal impedances from the renal and iliac arteries are known to affect the pulsatile flow waveforms in the infrarenal aorta. Physiologically, the aorta can experience a large increase in flow when comparing rest and exercise conditions.

Rest Conditions. The measurements of unsteady velocity in the abdominal aorta has revealed similar flow charateristics as were seen with flow visualization.

In the suprarenal aorta, the flow was relatively undisturbed throughout the cardiac cycle and exhibited a laminar type pattern which accelerated and decelerated regularly as depicted in Figure 1. The velocity profiles were regular and approximately parabolic throughout the cardiac cycle. The velocity across the vessel was forward throughout most of the cardiac cycle. There was a small degree of flow reversal at the vessel wall during late systole which was evenly distributed around the circumference of the tube. The centerline velocity oscillated between 5 and 30 cm/s. Velocity at the walls varied between -1 and 5 cm/s with reverse velocity appearing only for 1/8 of the cardiac cycle. The time-averaged mean velocities for the points near the left and right walls was 0.38 and 0.88 cm/s, respectively.

In contrast, the velocity patterns in the infrarenal aorta exhibited more complex velocity patterns that varied over the cardiac cycle (See Figure 2). In systole, the velocity profiles were basically parabolic with a centerline maximum velocity of 33 cm/s. In late systole, the flow near the walls definitely reversed, giving the velocity profile sinusoidal shape. Velocity reversal was stronger along the posterior wall when compared with the rest of the artery wall at the mid-point of the abdominal aorta. The reverse velocities reached -15 cm/s near the posterior wall at end-systole at a point approximately 2 mm from the posterior wall. The mean velocity near the posterior wall was -3.4 cm/s, while the mean velocity near the anterior wall was 1.7 cm/s. Reverse velocity persisted at the posterior wall for most of diastole giving rise to negative shears over 75% of the cardiac cycle at this location. Velocity reversal along the anterior wall was less pronounced and lasted over 44% of the cardiac cycle.

Toward the aortic bifurcation, reverse velocities shifted from the posterior wall toward the lateral walls. A contour plot of negative velocity distribution throughout the cross-section of the lumen is shown in Figure 3. The maximum velocity was located near the lateral walls. Negative velocities reached -14 cm/s at the left-posterior portion of the vessel. Mean velocities at the anterior and posterior walls were 3.2 and 1.6 cm/s, respectively. The velocities were reversed near the wall for approximately 25% of the cardiac cycle except for the lateral walls where velocity was negative for more than 50% of the cycle. The measurements confirmed the visualization findings that the separation region along the posterior wall of the abdominal aorta divides at the aortic bifurcation and then localizes to the lateral walls.

Relationship to atherosclerosis. An association appears to be present in our model of the human abdominal aorta between the hemodynamic conditions of low mean, oscillatory wall shear stress and high residence time and infrarenal atherosclerosis. While strongly implying that the posterior wall is the initial site of atherogenesis in the infrarenal aorta, this conclusion cannot be made without detailed correlation with morphologic measurements. It is interesting to note that the distribution of raised lesions in aortas obtained from young individuals with traumatic accidents are located in the same posterior area of high residence time as predicted from our model (Cornhill - PDAY study).

A comparison of the quantitative velocity measurements will be performed against the quantitative morphometry of atherosclerotic lesions. This correlation should aid in defining exactly which hemodynamic factors most strongly contribute to the localization of atherosclerotic plaque in the human aorta.

3. The protocols for human subjects have not changed.

4. No vertebrate animal studies are involved.

5. Publications.

Attached. Three additional manuscripts have been submitted or drafted.

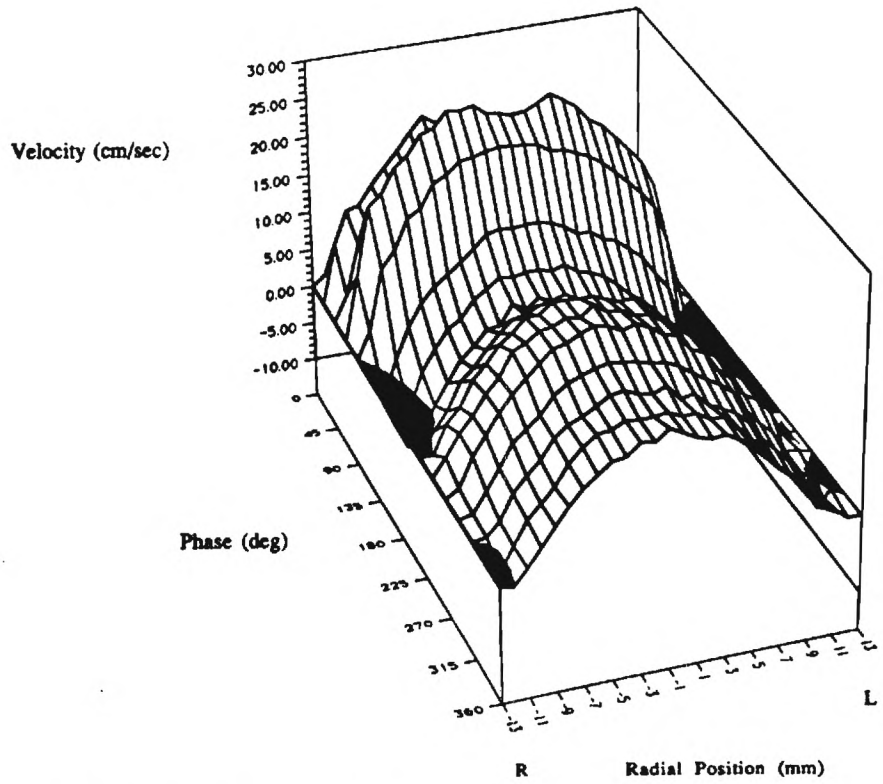

Fig. 1 Velocity profile in the coronal plane as a function of time in the suprarenal aorta. L denotes the left wall, and R denotes the right wall. The shaded areas correspond to negative velocities. The small amount of flow reversal is confined to the region near the wall in diastole.

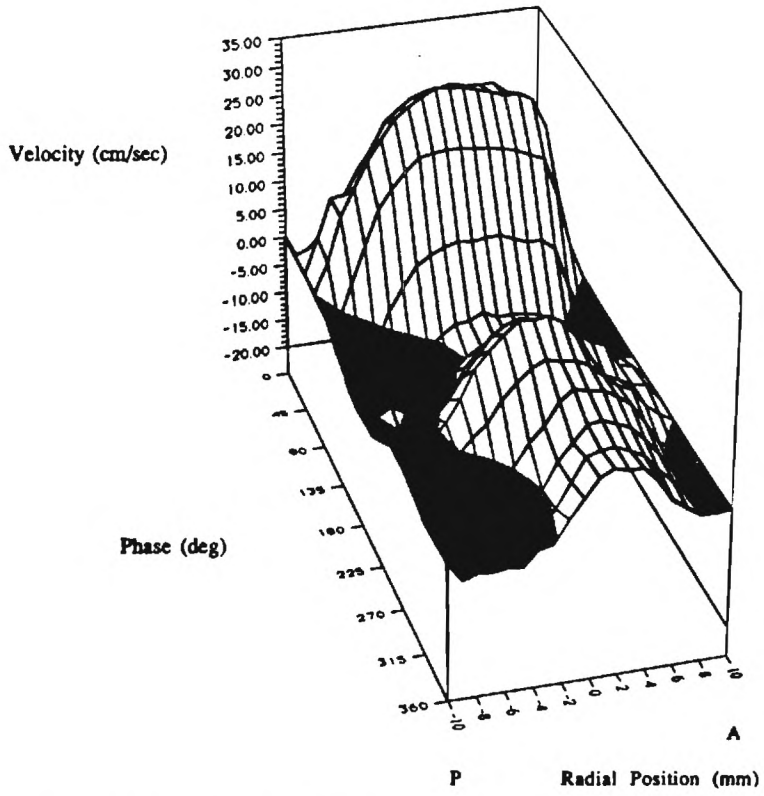

Fig. 2 Velocity profile in the sagittal plane as a function of time 12 mm distal to the left renal artery. A denotes the anterior wall, and P denotes the posterior wall. The shaded areas of reverse flow are most prevalent along the posterior wall.

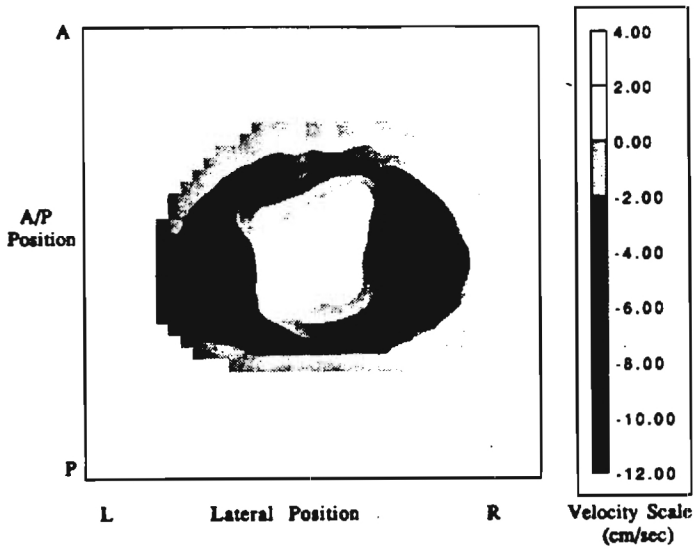

Fig. 3 Contour plot of the two dimensional velocity profile 11 mm proximal to the flow divider in the aortic bifurcation at end systole. The darker areas correspond to regions of the most negative velocities. There is more reversal along the lateral posterior walls.